

ABSTRACTS:

STUDIES OF DNA COVALENT MODIFICATIONS BY MASS SPECTROMETRY

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A stable isotope labeling HPLC-ESI/MS/MS approach was developed to map the formation of guanine adducts induced by tobacco carcinogens, e.g. 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) and benzo[a]pyrene, within DNA sequences. $^{15}\text{N}_3$ -labeled guanine was incorporated at specific sites within DNA duplexes derived from the *K-ras* protooncogene and p53 tumor suppressor gene, followed by carcinogen treatment and HPLC-MS/MS analysis to determine adduct yields at the labeled position. Our results indicate that the reactivity of a given base towards activated tobacco carcinogens is affected by sequence context, endogenous cytosine methylation, and the nature of the DNA modifying agent. The applicability of this approach to structural studies of DNA modifications by bifunctional electrophiles is demonstrated.

STUDIES OF PROTEIN MODIFICATIONS BY MASS SPECTROMETRY

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With the development of electrospray and matrix assisted laser desorption ionization techniques, mass spectrometry has become the primary tool for the characterization of biopolymers. Combined with two dimensional high resolution liquid chromatography, tandem mass spectrometry (quadrupole-quadrupole, or quadrupole - time of flight) has become an analytical technique by which components of extremely complex mixtures can be resolved and each component uniquely identified. This instrumentation is exceptionally powerful for the characterization of complex mixtures of proteins/peptides. Further, by using stable isotope tagging, proteins from one source (plant, animal, etc.) can be distinguished from those of another source. The difference in the relative proportion of proteins indicates stress (physical/chemical) being placed on one of the sources. Examples obtained from research being conducted at the University of Minnesota St. Paul, Minneapolis, and Duluth campuses will be used to explain how these analyses are done, and demonstrate how they are being applied to solve complex problems in pharmacology, toxicology, and ecology.